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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,196	01/24/2002	Y. Tom Tang	039386-0220	3875

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/744,196	TANG ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response and amendment filed July 12, 2007 is acknowledged and entered. Claims 3-11 are pending and under examination.

Response to Arguments

2. The rejection of claims 3-11 under 35 U.S.C. 101 for not being supported by either a specific, substantial and credible asserted utility, or a well-established utility, is withdrawn in view of Applicant's persuasive arguments. The accompanying rejection of claims 3-11 under 35 U.S.C. 112, first paragraph, is also withdrawn.

Claims Summary

3. The claims are drawn to an isolated polynucleotide encoding a polypeptide comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 2, wherein the polypeptide is associated with a cell proliferation disease. Also claimed is a polynucleotide comprising a sequence having at least 95% sequence identity to SEQ ID NO: 7, wherein the polynucleotide encoding a polypeptide associated with a cell proliferation disease.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

(*New Rejection*) Claims 3-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention. The claims indicate that the encoded polypeptide is associated with a cell proliferation disease. It is unclear from the claims and the specification what relationship exists between the polypeptide and the associated cell proliferation disease. How is the polypeptide associated with a cell proliferation disease? Without an understanding of the relationship between the polypeptide and the disease, the meaning of the term "associated" renders indefinite the scope of the polynucleotide encoding the polypeptide. The identification of a polynucleotide that encodes a polypeptide that is at least 95% identical to SEQ ID NO: 2, or a polynucleotide that is at least 95% identical to SEQ ID NO: 7, and is associated with a cell proliferation disease, relies on the association itself. Absent the knowledge of the particulars of the association, one cannot determine the metes and bounds of the claimed polynucleotide.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(*New Rejection*) Claims 3-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a polypeptide comprising SEQ ID NO: 2, does not reasonably provide enablement for an isolated polynucleotide encoding a polypeptide having at least 95% sequence identity to SEQ ID NO: 2 wherein the polypeptide is associated with a cell proliferation disease. Similarly, the specification is enabling for an isolated polynucleotide comprising SEQ ID NO: 7, but is not enabling for a polynucleotide that is 95% identical to SEQ ID NO: 7 and encodes a polypeptide associated with a cell proliferation disease. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims encompass polynucleotides encoding SEQ ID NO: 2, wherein the polypeptide of SEQ ID NO: 2 is associated with any cell proliferation disease. In another embodiment, the claims encompass polynucleotides encoding polypeptides having 95% identity to SEQ ID NO: 2, wherein the polypeptides are associated with any cell proliferation disease. As discussed above in the rejection under 35 U.S.C., 112, second paragraph, the association of the polypeptide to the cell proliferation disease is essential in determining the identity of the polypeptide itself. It is unclear which variants qualify as the variants intended to be encompassed by the claims. In other words, while one of skill can make the polynucleotides that encode variants of SEQ ID NO: 2 as well as variant polynucleotides of SEQ ID NO: 7, one cannot determine whether those polynucleotides have encoded polypeptide variants that have an association with a cell proliferation disease.

The guidance in the specification discloses that MACP-2 (SEQ ID NO: 2) is expressed in tumor cells (page 14, lines 14-16, Table 3), such as prostate cancer tumor tissue. The specification also discloses, generally, sample assays for using polynucleotides, such as MACP-2, in diagnostic methods (page 34, line 20 through page 38, line 11). These assays/diagnostic methods do not provide specific types of proliferative diseases that are associated with MACP-2. Without this knowledge, one would not know what cell proliferative disease to use MACP-2 as a diagnostic marker. Even with regard to the expression of MACP-2 in prostate tumor tissue, Applicant has

determined whether the level of expression is significantly higher than the level of expression in normal prostate tissue.

The state of the art, post-filing, shows that MACP-2, also called WIF-1, is associated with proliferative disease, including cancer, and that detection of aberrant expression of WIF-1 is indicative of cancer. The levels of WIF-1 expression vary between types of cancer and stages of disease. Specifically, Applicant points to Steg *et al.* (*Molecular Diagnostics*, 8:76-83, 2006) which discloses that WIF-1 was expressed in tissues samples from 5/6 human ovarian endometriod adenocarcinomas, but was not expressed in normal ovarian tissue. Applicant also points to similar work in mice that demonstrated that WIF-1 was over-expressed in ovarian granulosa cell tumors and in solid pretumoral lesions in the ovaries of mice, compared with normal ovarian tissue. Boerboom *et al.* (*Cancer Res.*, 66:1964-1973 (2006), see abstract and pages 1964 and 1966). Further, WIF-1 over expression has also been observed in other cancer types, evidenced by Cebrat *et al.* (*Cancer Lett.*, 206:107-113, 2004), which demonstrated that WIF-1 was over expressed in intestinal adenomas compared to normal epithelial cells in APC mice, and was also over expressed in cell lines derived from murine and human mammary gland adenocarcinoma and human colon adenocarcinoma (page 107, 111). In another example, using lux reporter construct, Reguart *et al.*, (*Biochem. Biophys. Res. Comm.* 323:229-234, 2004) demonstrated increased transcription in human cell lines derived from colon and non-small-cell lung cancers, but not from mesothelioma.

The level of predictability with regard to the diagnostic capabilities of MACP-2 is limited to those examples listed above, since the polypeptide is novel and its functions are still being elucidated. As of the filing date of this application, the polypeptide was

only known to be involved in cell proliferation somehow, without any specific cell proliferation diseases clearly associated with the polypeptide. The post-filing data supports the assertion that the polypeptide is reasonably involved in cell proliferative diseases, at least its role as a diagnostic marker. However, these specific diseases with which MACP-2 has been associated with were discovered post-filing.

Given the breadth of the claims, the state of the art, the amount of guidance in the specification and limited predictability with regard to MACP-2, the specification does not adequately enable the full scope of the claims. While the polynucleotide that encodes SEQ ID NO: 2 is enabled, and the polynucleotide comprising SEQ ID NO: 7 is enabled, the claimed association of the polypeptide with any cell proliferative disease is not enabled, nor are the variant polypeptides that are defined by their association with any cell proliferative disease.

6. Claims 3, 5-7, and 9-11 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims encompass polynucleotides encoding sequences having at least 95% sequence identity to SEQ ID NO: 2, or polynucleotides having at least 95% identity to SEQ ID NO: 7, respectively, and fragments thereof. The polynucleotide sequences encode polypeptides that are associated with a cell proliferation disease. The specification does not provide adequate written description of the claimed genus for reasons of record.

Applicant's argument has been carefully considered but fails to persuade. Applicant argues that cancer is a cell proliferation disease, and MACP-2 is expressed in prostate tumor tissue and libraries of other proliferative diseased tissues (see Tables 1, 3 and 4). In response to Applicant's argument, the Office recognizes that MACP-2 is expressed in various cancerous tissues. However, the "association" that is claimed in relation to a cell proliferation disease is not clearly set forth in the specification, nor has Applicant identified any particular portion of SEQ ID NO: 2 that is essential to its association with a cell proliferative disease. Applicant has provided a partial structure (variant or fragment of SEQ ID NO: 2) and a general function (associated with a cell proliferative disease). The missing elements are: 1) a structure/function correlation, and 2) a clear understanding of the function of the variant or fragment of the polypeptide. With the information provided in the specification, one of skill in the art would be able to make *a* polynucleotide that encodes a polypeptide having 95% sequence identity to SEQ ID NO: 2, or *a* polynucleotide that is 95% identical to SEQ ID No: 7, or *a* polynucleotide that encodes a fragment of SEQ ID NO: 2. However, one would not be able to make the polynucleotide that Applicant is attempting to encompass by the claim language because the function is not correlated with the structure and the function is not clearly understood. Therefore, the claims remain rejected.

Conclusion

7. No claim is allowed. Allowable subject matter would be isolated polynucleotides encoding polypeptides comprising SEQ ID NO: 2, and isolated polynucleotides comprising SEQ ID NO: 7, without any functional language, percent identity, or

fragment language. An attempt to discuss this allowable subject matter with Michele Simpkin via telephone voice-recorded message was made on September 6, 2007, however, no reply was received as of September 11, 2007.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B. Chen/ 9-11-07
Primary Examiner, TC1600